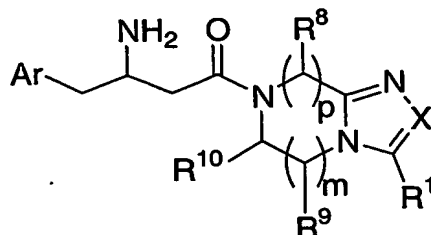


## WHAT IS CLAIMED IS:

1. A compound of structural formula I:



(I)

5 wherein

each n is independently 0, 1, or 2;

m is 1 or 2;

p is 1 or 2; with the proviso that m + p is 3;

X is N or CR<sup>2</sup>;

10

Ar is phenyl substituted with one to five R<sup>3</sup> substituents;

R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of

hydrogen,

15

halogen,

hydroxy,

cyano,

C<sub>1-10</sub> alkyl, wherein alkyl is unsubstituted or substituted with one to five substituents

independently selected from halogen or hydroxy,

20

C<sub>1-10</sub> alkoxy, wherein alkoxy is unsubstituted or substituted with one to five substituents

independently selected from halogen or hydroxy,

C<sub>1-10</sub> alkylthio, wherein alkylthio is unsubstituted or substituted with one to five substituents

independently selected from halogen or hydroxy,

C<sub>2-10</sub> alkenyl, wherein alkenyl is unsubstituted or substituted with one to five substituents

25

independently selected from halogen or hydroxy,

(CH<sub>2</sub>)<sub>n</sub>COOH,

(CH<sub>2</sub>)<sub>n</sub>COOC<sub>1-6</sub> alkyl,

(CH<sub>2</sub>)<sub>n</sub>CONR<sup>4</sup>R<sup>5</sup>, wherein R<sup>4</sup> and R<sup>5</sup> are independently selected from the group consisting of hydrogen, tetrazolyl, thiazolyl, (CH<sub>2</sub>)<sub>n</sub>-phenyl, (CH<sub>2</sub>)<sub>n</sub>-C<sub>3-6</sub> cycloalkyl, and C<sub>1-6</sub> alkyl, wherein alkyl is unsubstituted or substituted with one to five halogens and wherein phenyl and cycloalkyl are unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens; or R<sup>4</sup> and R<sup>5</sup> together with the nitrogen atom to which they are attached form a heterocyclic ring selected from azetidine, pyrrolidine, piperidine, piperazine, and morpholine wherein said heterocyclic ring is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens;

(CH<sub>2</sub>)<sub>n</sub>-NR<sup>4</sup>R<sup>5</sup>,

(CH<sub>2</sub>)<sub>n</sub>-OCONR<sup>4</sup>R<sup>5</sup>,

(CH<sub>2</sub>)<sub>n</sub>-SO<sub>2</sub>NR<sup>4</sup>R<sup>5</sup>,

(CH<sub>2</sub>)<sub>n</sub>-SO<sub>2</sub>R<sup>6</sup>,

(CH<sub>2</sub>)<sub>n</sub>-NR<sup>7</sup>SO<sub>2</sub>R<sup>6</sup>,

(CH<sub>2</sub>)<sub>n</sub>-NR<sup>7</sup>CONR<sup>4</sup>R<sup>5</sup>,

(CH<sub>2</sub>)<sub>n</sub>-NR<sup>7</sup>COR<sup>7</sup>,

(CH<sub>2</sub>)<sub>n</sub>-NR<sup>7</sup>CO<sub>2</sub>R<sup>6</sup>,

(CH<sub>2</sub>)<sub>n</sub>-COR<sup>6</sup>,

(CH<sub>2</sub>)<sub>n</sub>-C<sub>3-6</sub> cycloalkyl, wherein cycloalkyl is unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy, C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

(CH<sub>2</sub>)<sub>n</sub>-aryl, wherein aryl is unsubstituted or substituted with one to five substituents independently selected from halogen, cyano, hydroxy, NR<sup>7</sup>SO<sub>2</sub>R<sup>6</sup>, SO<sub>2</sub>R<sup>6</sup>, CO<sub>2</sub>H, C<sub>1-6</sub> alkyloxycarbonyl, C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

(CH<sub>2</sub>)<sub>n</sub>-heteroaryl, wherein heteroaryl is unsubstituted or substituted with one to three substituents independently selected from hydroxy, halogen, C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens, and

(CH<sub>2</sub>)<sub>n</sub>-heterocyclyl, wherein heterocyclyl is unsubstituted or substituted with one to three substituents independently selected from oxo, hydroxy, halogen, C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

wherein any methylene (CH<sub>2</sub>) carbon atom in R<sup>1</sup> or R<sup>2</sup> is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C<sub>1-4</sub> alkyl unsubstituted or substituted with one to five halogens;

5 each R<sup>3</sup> is independently selected from the group consisting of  
hydrogen,  
halogen,  
cyano,  
hydroxy,  
10 C<sub>1-6</sub> alkyl, unsubstituted or substituted with one to five halogens, and  
C<sub>1-6</sub> alkoxy, unsubstituted or substituted with one to five halogens;

R<sup>6</sup> is independently selected from the group consisting of tetrazolyl, thiazolyl, (CH<sub>2</sub>)<sub>n</sub>-phenyl, (CH<sub>2</sub>)<sub>n</sub>-  
C<sub>3-6</sub> cycloalkyl, and C<sub>1-6</sub> alkyl, wherein alkyl is unsubstituted or substituted with one to five halogens  
15 and wherein phenyl and cycloalkyl are unsubstituted or substituted with one to five substituents  
independently selected from halogen, hydroxy, C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy, wherein alkyl and alkoxy  
are unsubstituted or substituted with one to five halogens, and wherein any methylene (CH<sub>2</sub>) carbon  
atom in R<sup>6</sup> is unsubstituted or substituted with one to two groups independently selected from halogen,  
hydroxy, C<sub>1-4</sub> alkyl, and C<sub>1-4</sub> alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one  
20 to five halogens;

each R<sup>7</sup> is hydrogen or R<sup>6</sup>;

each R<sup>8</sup>, R<sup>9</sup>, and R<sup>10</sup> is independently selected from the group consisting of  
25 hydrogen,  
cyano,  
carboxy,  
C<sub>1-6</sub> alkyloxycarbonyl,  
C<sub>1-10</sub> alkyl, unsubstituted or substituted with one to five substituents independently selected  
30 from halogen, hydroxy, C<sub>1-6</sub> alkoxy, carboxy,  
C<sub>1-6</sub> alkyloxycarbonyl, and phenyl-C<sub>1-3</sub> alkoxy, wherein alkoxy is unsubstituted or  
substituted with one to five halogens,  
(CH<sub>2</sub>)<sub>n</sub>-aryl, wherein aryl is unsubstituted or substituted with one to five substituents  
independently selected from halogen, hydroxy, C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy, wherein  
35 alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

$(\text{CH}_2)_n$ -heteroaryl, wherein heteroaryl is unsubstituted or substituted with one to three substituents independently selected from hydroxy, halogen,  $\text{C}_{1-6}$  alkyl, and  $\text{C}_{1-6}$  alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

$(\text{CH}_2)_n$ -heterocyclyl, wherein heterocyclyl is unsubstituted or substituted with one to three substituents independently selected from oxo, hydroxy, halogen,  $\text{C}_{1-6}$  alkyl, and  $\text{C}_{1-6}$  alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

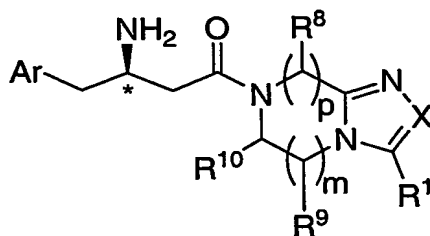
$(\text{CH}_2)_n$ - $\text{C}_{3-6}$  cycloalkyl, wherein cycloalkyl is unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy,  $\text{C}_{1-6}$  alkyl, and  $\text{C}_{1-6}$  alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens, and

$(\text{CH}_2)_n\text{CONR}^4\text{R}^5$ , wherein  $\text{R}^4$  and  $\text{R}^5$  are independently selected from the group consisting of hydrogen, tetrazolyl, thiazolyl,  $(\text{CH}_2)_n$ -phenyl,  $(\text{CH}_2)_n$ - $\text{C}_{3-6}$  cycloalkyl, and  $\text{C}_{1-6}$  alkyl, wherein alkyl is unsubstituted or substituted with one to five halogens and wherein phenyl and cycloalkyl are unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy,  $\text{C}_{1-6}$  alkyl, and  $\text{C}_{1-6}$  alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens;

or  $\text{R}^4$  and  $\text{R}^5$  together with the nitrogen atom to which they are attached form a heterocyclic ring selected from azetidine, pyrrolidine, piperidine, piperazine, and morpholine wherein said heterocyclic ring is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy,  $\text{C}_{1-6}$  alkyl, and  $\text{C}_{1-6}$  alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens;

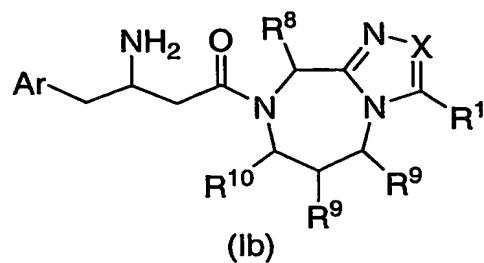
wherein any methylene  $(\text{CH}_2)$  carbon atom in  $\text{R}^8$ ,  $\text{R}^9$  or  $\text{R}^{10}$  is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and  $\text{C}_{1-4}$  alkyl unsubstituted or substituted with one to five halogens.

2. The compound of Claim 1 of structural formula Ia wherein the carbon atom marked with an \* has the *R* configuration:

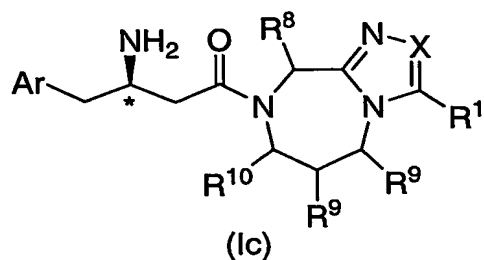


(Ia)

3. The compound of Claim 1 of structural formula Ib:

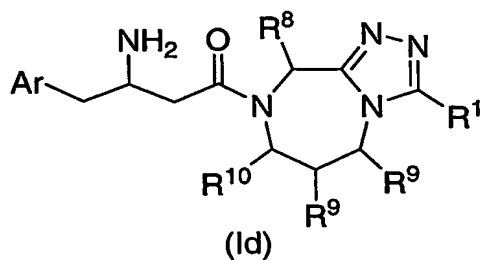


4. The compound of Claim 3 of structural formula Ic wherein the carbon atom marked with an \* has the *R* configuration

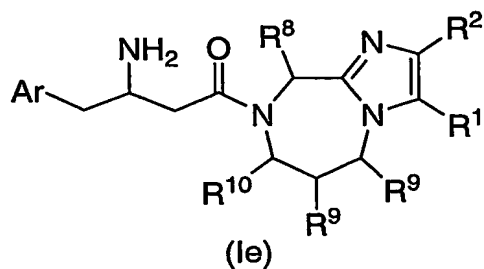


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5. The compound of Claim 3 of structural formula Id:

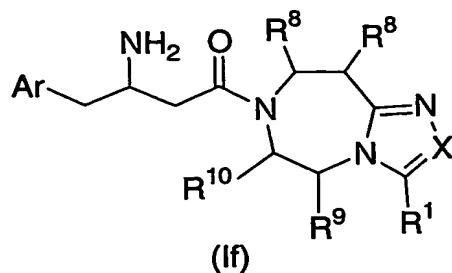


6. The compound of Claim 3 of structural formula Ie:

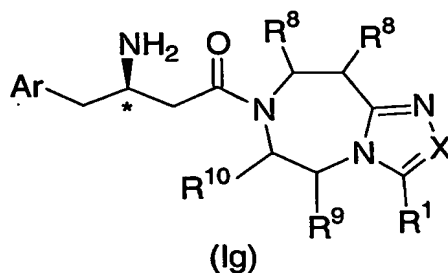


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7. The compound of Claim 1 of structural formula If:

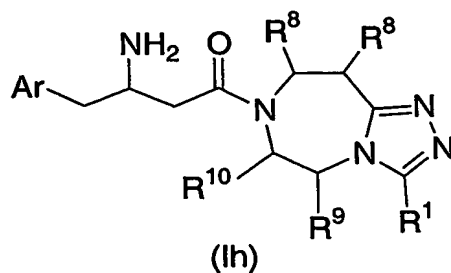


8. The compound of Claim 7 of structural formula Ig wherein the carbon atom marked with an \* has the *R* configuration:

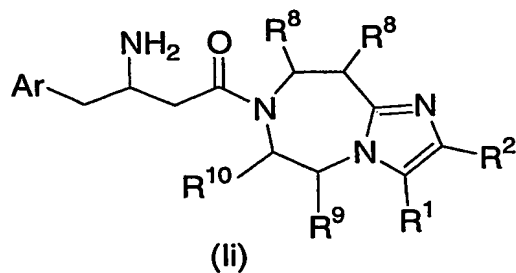


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9. The compound of Claim 7 of structural formula Ih:



10. The compound of Claim 7 of structural formula Ii:



11. The compound of Claim 1 wherein R<sup>3</sup> is selected from the group consisting of hydrogen, fluoro, chloro, bromo, trifluoromethyl, and methyl.

12. The compound of Claim 11 wherein  $R^3$  is selected from the group consisting of hydrogen, fluoro, and chloro

5 13. The compound of Claim 1 wherein  $R^1$  is selected from the group consisting of:  
hydrogen,  
halogen,  
 $C_{1-6}$  alkyl, wherein alkyl is unsubstituted or substituted with one to five substituents

independently selected from halogen or hydroxy,

10  $(CH_2)_n$ -aryl, wherein aryl is unsubstituted or substituted with one to five substituents

independently selected from halogen, CN, hydroxy,  $NR^7SO_2R^6$ ,  $SO_2R^6$ ,  $CO_2H$ ,  $C_{1-6}$  alkyloxycarbonyl,  $C_{1-6}$  alkyl, and

$C_{1-6}$  alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens;

15  $(CH_2)_n$ -heteroaryl, wherein heteroaryl is unsubstituted or substituted with one to three substituents independently selected from hydroxy, halogen,  $C_{1-6}$  alkyl, and  $C_{1-6}$  alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens, and wherein any methylene  $(CH_2)$  carbon atom in  $R^1$  is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and  $C_{1-4}$  alkyl unsubstituted or  
20 substituted with one to five halogens.

14. The compound of Claim 13 wherein  $R^1$  is selected from the group consisting of  
hydrogen,  
methyl,  
25 trifluoromethyl,  
phenyl,  
4-fluorophenyl,  
4-(trifluoromethyl)phenyl,  
4-(trifluoromethoxy)phenyl, and  
30 5-methyl-1,3,4-oxadiazol-2-yl.

15. The compound of Claim 1 wherein  $R^2$  is selected from the group consisting of  
hydrogen,  
halogen, and

C<sub>1-6</sub> alkyl, wherein alkyl is unsubstituted or substituted with one to five substituents independently selected from halogen or hydroxy.

5 16. The compound of Claim 15 wherein R<sup>2</sup> is selected from the group consisting of hydrogen and trifluoromethyl.

17. The compound of Claim 1 wherein R<sup>8</sup>, R<sup>9</sup>, and R<sup>10</sup> are independently selected from the group consisting of:

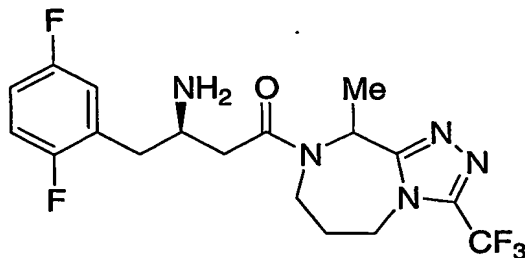
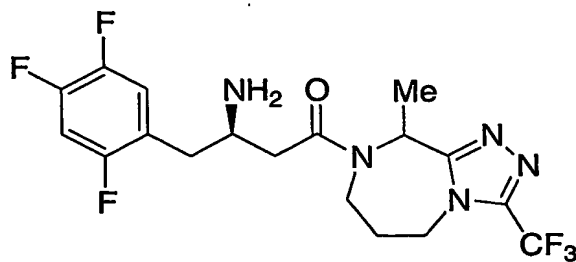
hydrogen and

10 C<sub>1-6</sub> alkyl, unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C<sub>1-6</sub> alkoxy, and phenyl-C<sub>1-3</sub> alkoxy, wherein alkoxy is unsubstituted or substituted with one to five halogens.

15 18. The compound of Claim 17 wherein R<sup>8</sup>, R<sup>9</sup>, and R<sup>10</sup> are each independently selected from the group consisting of hydrogen and methyl.

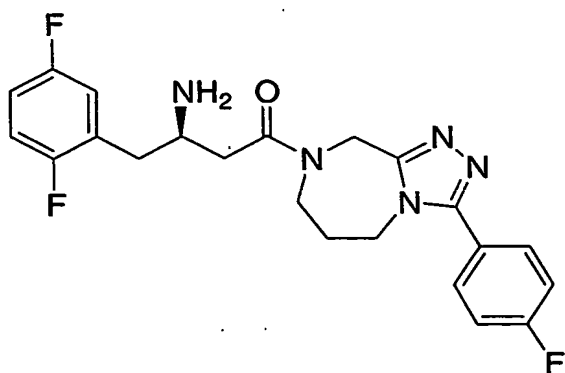
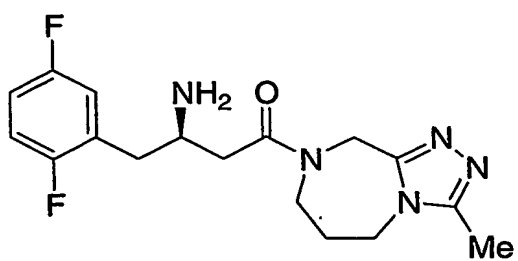
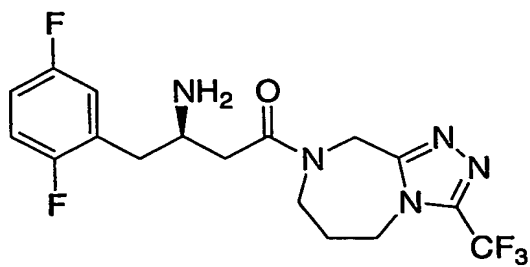
19. The compound of Claim 18 wherein R<sup>9</sup> and R<sup>10</sup> are hydrogen.

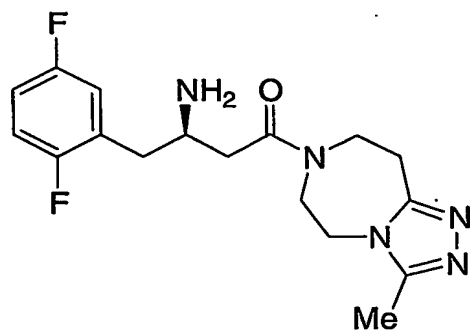
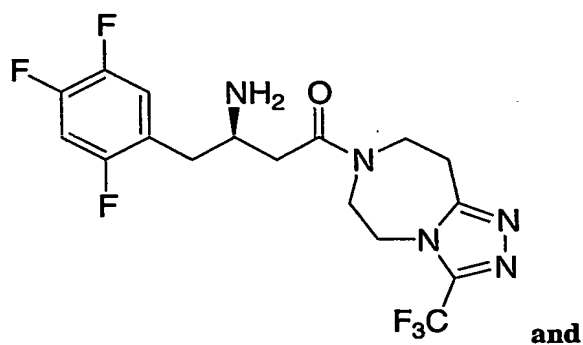
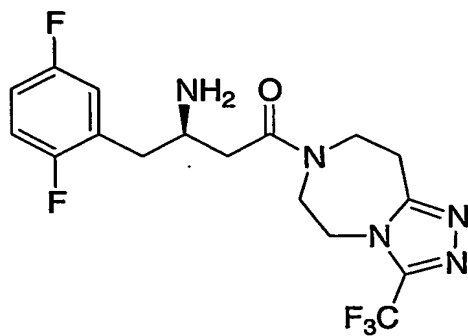
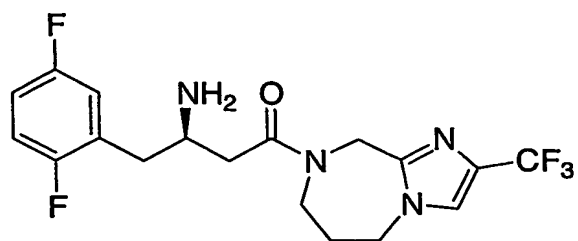
20. The compound of Claim 2 which is selected from the group consisting of:



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or a pharmaceutically acceptable salt thereof.

21. A pharmaceutical composition which comprises a compound of Claim 1 and a pharmaceutically acceptable carrier.

22. A method for treating diabetes in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

23. A method for treating non-insulin dependent (Type 2) diabetes in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

24. A method for treating hyperglycemia in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

25. A method for treating obesity in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

26. A method for treating one or more lipid disorders selected from the group of dyslipidemia, hyperlipidemia, hypertriglyceridemia, hypercholesterolemia, low HDL and high LDL in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

27. A method for treating in a mammal in need thereof one or more conditions selected from the group consisting of (1) hyperglycemia, (2) low glucose tolerance, (3) insulin resistance, (4) obesity, (5) lipid disorders, (6) dyslipidemia, (7) hyperlipidemia, (8) hypertriglyceridemia, (9) hypercholesterolemia, (10) low HDL levels, (11) high LDL levels, (12) atherosclerosis and its sequelae, (13) vascular restenosis, (14) irritable bowel syndrome, (15) inflammatory bowel disease, including Crohn's disease and ulcerative colitis, (16) other inflammatory conditions, (17) pancreatitis, (18) abdominal obesity, (19) neurodegenerative disease, (20) retinopathy, (21) nephropathy, (22) neuropathy, (23) Syndrome X, (24) ovarian hyperandrogenism (polycystic ovarian syndrome), and other disorders where insulin resistance is a component, wherein the method comprises the administration to the mammal a therapeutically effective amount of a compound of Claim 1.

28. The pharmaceutical composition of Claim 21 further comprising one or more additional active ingredients selected from the group consisting of:

- (a) a second dipeptidyl peptidase IV inhibitor;
- (b) an insulin sensitizer selected from the group consisting of a PPAR $\gamma$  agonist, a PPAR $\alpha/\gamma$  dual agonist, a PPAR $\alpha$  agonist, a biguanide, and a protein tyrosine phosphatase-1B inhibitor;
- 5 (c) an insulin or insulin mimetic;
- (d) a sulfonylurea or other insulin secretagogue;
- (e) an  $\alpha$ -glucosidase inhibitor;
- (f) a glucagon receptor antagonist;
- (g) GLP-1, a GLP-1 mimetic, or a GLP-1 receptor agonist;
- 10 (h) GIP, a GIP mimetic, or a GIP receptor agonist;
- (i) PACAP, a PACAP mimetic, or a PACAP receptor agonist;
- (j) a cholesterol lowering agent such as (i) HMG-CoA reductase inhibitor, (ii) sequestrant, (iii) nicotiny alcohol, nicotinic acid or a salt thereof, (iv) PPAR $\alpha$  agonist, (v) PPAR $\alpha/\gamma$  dual agonist, (vi) inhibitor of cholesterol absorption, (vii) acyl CoA:cholesterol acyltransferase inhibitor, and
- 15 (viii) anti-oxidant;
- (k) a PPAR $\delta$  agonist;
- (l) an antiobesity compound;
- (m) an ileal bile acid transporter inhibitor;
- (n) an anti-inflammatory agent; and
- 20 (o) an antihypertensive agent.

29. The pharmaceutical composition of Claim 28 wherein the PPAR $\alpha/\gamma$  dual agonist is KRP-297.

25 30. A method of treating diabetes in a mammal in need thereof comprising administering to the mammal a therapeutically effective amount of a compound of Claim 1 in combination with the PPAR $\alpha/\gamma$  dual agonist KRP-297.